

### **REMARKS**

In an Office Action mailed December 12, 2006, the Examiner in charge of the application acknowledged applicants timely filing of an RCE and withdrew the finality of the previous Office Action. The Examiner correctly stated the status of the claims; claims 1, 3, 7, 9, 10, 12, 13, 15 and 16 are pending and are under consideration.

The Examiner withdrew rejections under 35 U.S.C. §102(b) and under 35 U.S.C. §102(e) in view of applicants' prior response. The Examiner imposed new grounds of rejection under 35 U.S.C. §112, second paragraph for indefiniteness and under 35 U.S.C. §103 for obviousness over Priori et al. (1996) in view Gepstein et al. For the reasons noted below, applicants respectfully traverse the new grounds of rejection and request reconsideration. Each ground of rejection is considered separately below.

#### **Rejections under 35 U.S.C. §112, second paragraph**

The claims stand rejected as indefinite for lack of clear antecedent basis for the recitation of "the agent." The preambles of the independent claims are amended to recite "A method for testing an agent" Reconsideration is respectfully requested.

#### **Rejections under 35 U.S.C. §103**

All claims stand rejected under 35 U.S.C. §103 over Priori in view of Gepstein. Applicants respectfully traverse the rejections because the combination does not yield the claimed invention. This combination rejection requires both cited documents. Notably, the Examiner looks to Gepstein to show isolating cardiomyocytes from human embryonic stem (hES) cells, which is absent from Priori, who tested guinea pig ventricular cardiomyocytes. However, nothing in Gepstein teaches the skilled person that a culture of differentiated hES cells would include all cardiomyocyte types. Gepstein did not assess the developmental potential of the obtained cardiomyocytes to form a range of cardiomyocyte types and, unlike Applicants, did not demonstrate the presence of such a range of cell types. Indeed, Gepstein noted at page 14 that its early-stage cardiomyocytes "did not reach the fully mature adult phenotype during the observation period." In contrast, Applicants state in paragraphs 43-46 of specification as filed that their cultures included distinct populations of cardiomyocytes with properties typical of nodal, atrial and ventricular cardiomyocytes.

Developmentally, early stage cardiomyocytes are characterized by a nodal-type action potential waveform. Although other work identified multiple cardiomyocyte types in cultures of differentiated mouse embryonic stem cells, nothing in the cited art establishes whether cultures of differentiated hES cells would or would not likewise contain multiple types. In addition to this shortcoming in the cited art, at least two factors raise significant uncertainty that multiple types would emerge in hES-derived cultures. First, the skilled artisan is well familiar with developmental differences between mice and humans; Gerstein et al. reinforce this point in the first paragraph of the Discussion on page 10, and again on page 13, of their application. Distinct species-specific components support mouse and hES cells in culture and direct differentiation of those cells. The cited art does not consider whether the species-specific factor profiles are available, and if so, whether they contribute, positively or negatively, to differentiation in culture of these distinct cells. Still further, species-specific differences in gestational term between mouse and human raise doubts as to whether the differentiated cells can develop further in culture to include atrial and ventricular cardiomyocyte types.

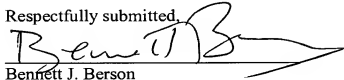
The Examiner cannot ignore the shortcomings and uncertainties in deciding that Gepstein closes the acknowledged gap between Priori and the claimed invention in which cultures derived from human embryonic stem cells contain a plurality of distinct cardiomyocyte populations having attributes of nodal, atrial and ventricular types. Because the skilled artisan in possession of Gepstein would have had no reasonable expectation of success, the cited combination cannot support the new grounds of rejection.

Reconsideration is respectfully requested. A petition for an extension of time for one month accompanies this response so the response will be deemed to have been timely filed. Should any additional extension of time be due, in this or in any subsequent response, please consider this to be a request for the appropriate extension of time and a request to charge the fee due to deposit account number 17-0055.

Application No.: 10/627,245  
Amendment Dated: April 11, 2007  
Reply to Office Action of December 12, 2006

No other fee is believed due. However, should another fee be due, in this or any subsequent response, please charge the fee to the same deposit account.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Bennett J. Berson", written over a horizontal line.

Bennett J. Berson  
Reg. No.: 37,094  
Attorney for Applicants  
QUARLES & BRADY LLP  
P.O. Box 2113  
Madison, WI 53701

TEL 608/251-5000  
FAX 608/251-9166